REMARKS

Reconsideration of the present application in light of the above amendments and the following remarks is respectfully requested. Claims 22-24 and 26-29 are pending. Claim 25 has been cancelled without prejudice to the future filing of divisional, continuation, or continuation-in-part applications. Claims 22-24 and 26-29 are amended without prejudice to pursue one aspect of the present invention. Support for the amendments can be found in the specification, in particular, at line 12, page 1 (IDDM definition), line 12, page 6 (QFA definition), Example 5 (QVAX). No new matter has been added to the application.

Rejection under 35 U.S.C. § 101

Claims 22-28 stand rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. In particular, the Action opposed the term "Use" in the claims. Applicants thank the Examiner for pointing out this oversight and for recommending amending the claims to read "A method of use". Accordingly, Applicants have amended the claims to read "A method of use", and respectfully request this rejection be withdrawn.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 22-28 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Action opposed the term "use" in Claims 22-28, "analogous or homologous" in Claim 22, "IDDM" or "QFA" in Claims 24 and 28, and the term "in the treatment" in Claim 22.

Applicants traverse this ground for rejection and submit the application distinctly claims the subject matter of the presently claimed invention. Applicants have amended Claims 22, 24, and 28 for clarification. Applicants submit one of skill in the art would fully understand the term "analogous or homologous" as in Claim 22, and from the extensive definition at line 7, page 7—line 26, page 9, to be components that are structurally or functionally similar to such components as *C. brunetii*, and are able to inhibit, delay or ameliorate autoimmune disease in a

mammal. Therefore, Applicants respectfully request this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 22-28 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for any antigenic component of any species of *Coxiella*, other than *Coxiella burnetii* in the manufacture of a medicament for the treatment of any autoimmune disease other than IDDM or autoimmune coxiellosis.

As an initial matter, Applicants thank the Examiner for stating the application is enabled for a method of use of a *Coxiella burnetti* in the manufacture of a medicament for treatment of IDDM or autoimmune coxiellosis in a mammal. With regard to the rejection of further enablement, however, Applicants respectfully traverse this ground for rejection.

Applicants submit, without acquiescing to the rejection, Claims 22-28 have been amended for clarification. Applicants further submit amended Claims 22-28 read on antigenic components of *Coxiella burnetii* or analogous or homologous components and are fully enabled by the instant specification. More specifically, Applicants submit one convenient way of screening for analogues or homologues is via anti-idiotypic antibody screening. For example, antibodies are raised to particular antigenic components of *C. burnetii* and anti-idiotypic antibodies raised to the first mentioned antibodies. The anti-idiotypic antibodies are then used to screen for molecules capable of binding or otherwise interacting with these antibodies. Support for the antigenic components of *C. burnetii* or analogous or homologous components can be found in the instant specification at Examples 1-5, pages 19-24, as well as lines 16-20, page 6, and lines 10-20, page 7.

Applicants further submit one of skill in the art would consider determining specific antigenic components of *C. burnetii* or analogous or homologous components to be routine experimentation, and not undue experimentation. Applicants submit such routine experimentation of generating polyclonal and monoclonal antibodies in a laboratory animal from bacterial components or whole cell lysates may require a fair amount of time, but not considerable skill. Furthermore, the state of the art and the relative skill of one in the art, generating antibodies from bacterial components is standard practice. Thus, under a *Wands*

analysis, such experimentation would be considered routine experimentation. *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

Therefore, Applicants respectfully request this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. §102(b), (First Rejection)

Claims 22, 23, and 25-28 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Zhang *et al.*, Gajdosova *et al.*, or Williams *et al.* as evidenced by Levy *et al.*, or Roue *et al.* In particular, the Action states Zhang *et al.*, Gajdosova *et al.*, and Williams *et al.*, allegedly teach a method of making a composition of *Coxiella burnetii* for use as a vaccine against *C. burnetii* infection. Further, the Action states Levy *et al.* and Roue *et al.* allegedly teach Q fever may be associated with autoimmune disease.

Applicants respectfully traverse this ground for rejection and submit the Federal Circuit has held that a claim is anticipated only if each and every element of the claim is found expressly or inherently in a single prior art reference. *Verdegaal Bros., Inc. v. Union Oil Co. of Calif.*, 814 F.2d 628, 2 U.S.P.Q.2d 1051 (Fed. Cir. 1987). Applicants submit none of the prior art cited expressly or inherently describes a method of using one or more antigenic components of *C. burnetii* in the manufacture of a medicament for treatment of autoimmune disease in a mammal, as described in Claim 22 of the presently claimed invention. Applicants submit the cited prior art, namely Zhang *et al.*, Gajdosova *et al.*, and Williams *et al.*, do not disclose any information related to treatment of autoimmune disease in a mammal.

Applicants further submit neither Levy *et al.* nor Roue *et al.* remedies such deficiency. Instead, the investigation by Levy *et al.* of determining the incidence of two autoimmune markers in Q-fever (smooth muscle antibodies and cold agglutinins) found "No correlation between Q-fever and smooth muscle antibodies titers and kinetics...." (*See* lines 8-9, Abstract, Measurements and Main Results.) Further, Roue *et al.*, examined a single patient stricken by Q-fever and did NOT suffer from autoimmunity as a result of the disease. Applicants submit mere speculation of an association of autoimmune episodes with Q-fever does not anticipate the presently claimed invention of one or more antigenic components of *C. burnetii*

used in the manufacture of a medicament for treatment of autoimmune disease in a mammal. Accordingly, Applicants respectfully request this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. §102(b), (Second Rejection)

Claims 22-28 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Qin *et al.*, as evidenced by Vodkin *et al.*, and Edgington. In particular, the Action states Qin *et al.* allegedly discloses a composition containing *Mycobacterial* cell wall adjuvant (Complete Freund's adjuvant) for treating the development of type I diabetes in non-obese diabetic mice. The Action further states Vodkin *et al.*, and Edgington allegedly disclose the use of heat shock proteins of adjuvants in vaccines for treatment of autoimmunity. The Action maintains such heat shock proteins derived from *Mycobacteria* constitute "analogous or homologous" components in *C. burnetii.*

Applicants traverse this ground for rejection. Applicants maintain the cited prior art does not anticipate the presently claimed invention. Applicants submit the presently claimed invention reads on a method for using antigenic components of *C. burnetii* or analogous or homologous components in the manufacture of a medicament for treatment of autoimmune disease in a mammal, which is not disclosed in any of the cited prior art references. Applicants submit the cited prior art references read on general adjuvants, which one of skill in the art recognizes contain many components that may amplify any general immunological reaction.

Applicants submit immunostimulation of non-obese diabetic mice by Complete Freund's Adjuvant does not completely block the autoimmune response, instead the response is converted from a destructive into a non-destructive form of auto-immunity (*See* lines 19-23, page 3 of the instant specification). Thus, functionally Complete Freund's Adjuvant does not prevent or reverse autoimmunity directed against islet tissue in diabetic mice. Applicants submit Example 3 demonstrates that QFA, an antigenic component of *C. brunetii*, is more efficacious than Complete Freund's Adjuvant at protecting beta cells from autoimmune destruction in non-obese diabetic mice. Applicants submit the presently claimed invention fulfills the long-felt need in the art for an agent capable of blocking autoimmune disease without the side effects of skin and gastrointestinal lesions, which occur with treatment of Complete Freund's Adjuvant. Thus,

Applicants submit the cited prior art does not anticipate the presently claimed invention and respectfully request this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 22-28 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Qin *et al.*, in view of Vodkin *et al.*, and Edgington and Barnes *et al.* In particular, the Action states Qin *et al.* allegedly teaches a method of producing a therapeutic composition of Complete Freund's Adjuvant for treating against the development of type I diabetes. The Action concedes, however, that Qin *et al.* does not teach the antigenic component contained in Complete Freund's Adjuvant is "analogous or homologous" to an antigenic component of *C. burnetii*. The Action alleges Vodkin *et al.* remedies the deficiency by teaching that immunogenic heat shock protein antigen of *C. burnetii* is "homologous" to a heat shock protein of *Mycobacterium* such that it could be used as a vaccine against Q-fever. The Action further alleges Edgington teaches Complete Freund's Adjuvant contains a mixture of heat shock proteins and the association of heat shock proteins with diabetes is "uninformed." The Action further alleges Barnes *et al.* discloses disadvantages of using Complete Freund's adjuvant for *in vivo* use due to lesions that form at the site of injection. The Action concludes it would allegedly have been obvious for one of skill in the art to combine the cited prior art to arrive at the presently claimed invention.

Applicants respectfully traverse this ground for rejection. Applicants thank the Examiner for noting Qin *et al.*, does not teach that the antigenic component contained in Complete Freund's Adjuvant is analogous or homologous to an antigenic component of *C. burnetii*, and submit none of the cited prior art corrects this deficiency.

Applicants submit the Action fails to establish a *prima facie* case of obviousness because nothing in the cited prior art provides the desirability or motivates one of skill in the art to combine the relevant teachings of the cited prior art. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Applicants submit Qin *et al.*, and Vodkin *et al.* fails to suggest or teach one of skill in the art the presently claimed invention, namely a method of antigenic components of *C. brunetii* or analogous or homologous components used in the manufacture of a

medicament for treatment of autoimmune disease in a mammal. Applicants submit none of the cited prior art, together or alone, obviates the presently claimed invention.

Applicants further submit Edgington teaches there is no evidence that administering Complete Freund's Adjuvant or heat shock proteins causes autoimmunity. Applicants submit this is unrelated to the presently claimed invention which demonstrates in Example 3 of the instant specification that the antigenic component of *C. brunetii*, QFA, is more efficacious than Complete Freund's Adjuvant at protecting beta cells from autoimmune destruction in non-obese diabetic mice. Applicants submit the presently claimed invention is more efficacious than other methods presently known in the art for delaying or inhibiting autoimmune disease, and provides significant benefits over the present state of the art, namely the lack of skin lesions at the site of injection.

Applicants submit Barnes *et al.* discloses the disadvantage of using Complete Freund's Adjuvant due to the skin lesions that form in the test animals. Applicants submit Barnes *et al.* does not suggest or motivate one of skill in the art to combine the cited prior art and arrive at the presently claimed invention. Applicants submit nothing in Barnes *et al.*, teaches or suggests a method of using antigenic components of *C. burnetii* or analogous or homologous components in the manufacture of a medicament for treatment of autoimmune disease in a mammal. Even assuming *arguendo*, Applicants submit Barnes *et al.*, may at best provide an "obvious to try" disclosure, which is not the standard of obviousness for patentability, according to the Federal Circuit. *In re Geiger*, 815 F.2d 686, 2 U.S.P.Q.2d (BNA)1276 (Fed.Cir. 1987). Applicants submit that hindsight reconstruction may indicate a need for agents other than Complete Freund's Adjuvant due to the high incidence of skin lesions, however nothing in the cited prior art teaches or suggests the use of antigenic components of *C. burnetii* for the treatment of autoimmune disease in a mammal. Thus, Applicants respectfully submit the Action fails to establish a *prima facie* case of obviousness and respectfully request this rejection be reconsidered and withdrawn.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 3, page 1, has been amended as follows:

~~This application is a continuation of pending United States Patent Application No. 09/142,597, filed March 5, 1999; which application was a U.S. Nation Stage application based off of PCT Application No. PCT/AU97/00161, filed on March 14, 1997; which application claims priority to Australian Patent Application No. PN 8703, filed March 14, 1996.~~

The instant application is a continuation of application SN 09/142,597, filed 03/05/1999, now pending, which is a 371 of PCT/AU97/00161, filed 03/14/1997 and claims foreign priority to application, PN 8703, filed 03/14/1996 in Australia.

The following subheading has been added at line 13, page 18:

Brief Summary of the Invention:

In the Claims:

Claim 25 has been canceled.

Claims 22, 23, 24, and 26-28 have been amended to read as follows:

22. (Amended) ~~Use~~ A method of use of ~~a species of~~ *Coxiella burnetii* or one or more antigenic ~~component~~ components therefrom or analogous or homologous components thereof in the manufacture of a medicament ~~in~~ for the treatment of an autoimmune disease in a mammal.

23. (Amended) ~~Use~~ A method according to claim 22 wherein the mammal is human or laboratory test animal.

24. (Amended) ~~Use~~ A method according to claim 23 wherein the autoimmune disease is insulin-dependent diabetes mellitus (IDDM).

26. (Amended) ~~Use~~ A method according to claim 23 wherein the *C. burnetii* is in the form of a killed preparation.

27. (Amended) ~~Use~~ A method according to claim 26 wherein the antigenic component is a Q fever antigen.

28. (Amended) ~~Use~~ A method according to claim 26 wherein the Q fever antigen is Q fever complement fixing antigen phase I (QFA).

New claim 29 as been added to read as follows:

29. (New) A method according to claim 26 wherein the antigenic component is a Q fever vaccine (QVAX).